

CONDENSATION OF 1,3-DIPHENYLPROPANETRIONE-1,2,3  
WITH ACTIVE METHYLENE COMPOUNDS

by

ROBERT ELLIOTT YEAGER

B. A., Southwestern College, Winfield, 1950

---

A THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Chemistry

KANSAS STATE COLLEGE  
OF AGRICULTURE AND APPLIED SCIENCE

1952

Docu-  
ments  
LD  
2668  
T4  
1952  
V4  
c.2

## TABLE OF CONTENTS

INTRODUCTION	1
EXPERIMENTAL	4
Preparation of Starting Materials	4
Condensation Reactions of 1,3-Diphenylpropanetri- one-1,2,3	6
Structure Studies on the Condensation Product of 1,3-Diphenylpropanetrione-1,2,3 and p-Nitro Benzyl Cyanide	15
Structure Studies on the Condensation Product of 1,3-Diphenylpropanetrione-1,2,3 and Malonic Acid	17
Structure Studies of Products Resulting from Various Condensation Reactions	20
DISCUSSION AND CONCLUSIONS	21
SUMMARY	28
ACKNOWLEDGMENTS	30
LITERATURE CITED	31

07-24-52 4-

## INTRODUCTION

Mechanisms of the reactions of tricarbonyl compounds are interesting and differ from those of monofunctional groups. This is particularly true when the functional groups are contiguous and the interaction of neighboring groups must be considered. A study of this deviation of chemical conduct to the behavior of a similar group when uninhibited by such influences is considered worthwhile due to the abundance of polyfunctional organic compounds.

Vicinal tricarbonyl compounds (I) (Table 1) are a group of chemically related substances containing three adjacent carbonyl groups.

Table 1. Representative tricarbonyl compounds.

---



---

	O	O	O
(I)	$R - C - C - C - R'$		
(II)	$R = R' = C_6H_5-$		
(III)	$R = R' = CH_3-$		
(IV)	$R = C_6H_5-; R' = CH_3-$		
(V)	$R = CH_3-; R' = -OC_2H_5$		
(VI)	$R = R' = -OC_2H_5$		
(VII)	$R = C_6H_5; R' = -OC_2H_5$		

---

The adjacent carbonyl groups may all be ketone groups, or a combination of ketone groups, and ester functional groups. The carbonyl of the ester groups would have different properties than those of the keto grouping.

The first reported synthesis of a tricarbonyl compound was reported by de Neufville and von Peckmann (10) who prepared 1,3-diphenylpropanetrione-1,2,3 (II) in 1891. Sachs and Barschall (11) prepared pentanetrione-2,3,4 (III) in 1901 and the synthesis of 1-phenylbutanetrione-1,2,3 (IV) was first reported by Sachs and Rohmer (12) in 1902. The mixed ester-diketone type molecule, ethyl 2,3-dioxobutanoate (V) was first prepared by Bouveault (4). In 1930 Bouveault and Wahl (5) oxidized malonic ester to diethyl mesoxalate (VI). Wahl (20) prepared 3-phenyl-2,3-dioxopropanoate (VII) in 1907.

Methods for preparing triketones use  $\beta$ -diketones as starting materials. The conversion of the active methylene group to a keto group may be accomplished by bromination and hydrolysis, oxidation, or condensation with nitroso compounds and hydrolysis. All procedures yield the hydrate of the triketones. A pure anhydrous product is obtained by vacuum distillation.

Triketones are oxidized easily by permanganate solutions and exhibit general reducing properties. Sensitivity to basic reagents is exemplified by diphenyltriketone, which is broken down into benzoic acid, benzoin, mandelic acid and carbon dioxide when treated with dilute sodium hydroxide. This change

has been compared to the benzil-benzilic acid rearrangement (10). It has been reported that these same compounds are degraded in a similar way when treated with sulfuric acid. Under such treatment the diphenyl compound is changed to benzil (16). Sharp and Hoffman (18) confirmed this observation by acidification of a base-refluxed mixture and by pyrolysis with water in a sealed tube. They obtained benzoic acid and benzil in both cases. It is assumed that hydrates of all vicinal triketone compounds are formed by the addition of the elements of water to the central carbonyl group.

There are no reported reactions of triketones with such carbonyl reagents as hydrogen cyanide or Schiff's reagent. However, in most cases they react with orthophenylenediamine to form quinoxalines. This is a specific reaction for compounds containing at least two contiguous carbonyl groups.

Selective reactivity of the middle carbonyl group of diphenyltriketone has been demonstrated by catalytic reduction with molecular hydrogen (3) to give dibenzoylcarbinol, and its condensation with phenylhydrazine (10) to give a phenylhydrazone.

Condensations of vicinal tricarbonyl compounds with active methylene compounds have been reported by Sachs and Herold (14), Sachs and Wolff (13), Sachs and Rohmer (12), and Schmitt (15). More recently, Sharp and Hoffman (18) successfully condensed 1,3-diphenylpropanetrione-1,2,3 with malonic acid and also with p-nitrophenylacetonitrile.

Structures postulated for the products obtained using modified Knoevenagel (6) reaction conditions need to be supported by additional evidence. Evidence in the literature (12, 13, 14, 15) of the structure of the products of such reactions has been obtained largely through analytical means.

It was believed that additional experimentation was necessary to provide a rigorous proof of the structure of products obtained from the condensation of active methylene compounds with tricarbonyl compounds. It was considered desirable to contribute to the general knowledge concerning vicinal tricarbonyl compounds. The information regarding the mechanisms of polyfunctional compounds with similar influencing contiguous groups was found also to be insufficient.

## EXPERIMENTAL<sup>1</sup>

### Preparation of Starting Materials

1,3-Diphenylpropanetrione-1,2,3. Approximately 100 gm were prepared during the course of the investigation. The procedures used are summarized below.

Benzalacetophenone was prepared by the method of Kohler and Chadwell (7). A yield of 427 gm, representing 93 per cent

---

<sup>1</sup> All melting points and boiling points were corrected for emergent stem. Temperatures are in degrees centigrade.

of the theoretical, was obtained from freshly distilled acetophenone (260 gm, 2.2 moles) and freshly distilled benzaldehyde (230 gm, 2.2 moles). The melting point ( $55-57^{\circ}$ ) agreed with that given by Kohler and Chadwell (7).

Benzalacetophenone dibromide was prepared according to the method of Allen (1). Benzalacetophenone (416 gm, 2.0 moles) was reacted with bromine (320 gm, 2.0 moles) in 1200 ml of  $\text{CCl}_4$ . The dibromide (600 gm, 82 per cent of theoretical) melted at  $156^{\circ}$ ; Allen (1) obtained a melting point  $156-157^{\circ}$ .

By the procedure of Allen (1), benzalacetophenonedibromide (552 gm, 1.5 moles) reacted with sodium methoxide (162 gm, 3.0 moles) in absolute methanol (1050 ml). Acid hydrolysis gave 199.5 gm (60 per cent of theoretical) of dibenzoylmethane, melting point  $77-78^{\circ}$ , in agreement with that reported by Allen (1).

Dibenzoylmethane (168 gm, 0.75 mole) reacted with bromine (85.5 ml, 1.59 moles) by the method of Bigelow and Hanslick (2) to give 217 gm (76 per cent of theoretical) of dibenzoyldibromomethane melting at  $94-95^{\circ}$  as reported by Bigelow and Hanslick (2).

Treatment of dibenzoyldibromomethane (227.2 gm, 0.54 mole) with fused potassium acetate (123.6 gm, 1.26 moles) in 426 ml of boiling glacial acetic acid, followed by cooling and hydrolysis in cold water, gave 142 gm (90 per cent of theoretical) of 1,3 diphenylpropanetrione-1,2,3 hydrate, melting at  $91^{\circ}$ .

The hydrate was distilled at reduced pressure to give a



light red oil which crystallized to 100 gm of yellow solid. This 1,3-diphenylpropanetrione-1,2,3 melted at 71-72° in agreement with Eigelow and Hanslick (2).

Condensation Reactions of  
1,3-Diphenylpropanetrione-1,2,3

Condensation of 1,3-Diphenylpropanetrione-1,2,3 with Malonic Acid. Application of Knoevenagel (6) conditions as modified by Sharp and Hoffman (18) yielded an addition compound.

Condensation was obtained by mixing cooled solutions of a mixture of pyridine (8.0 ml, 0.087 mole) and the triketone (5.43 gm, 0.0228 mole) and a mixture of piperidine (3.40 ml, 0.034 mole) and malonic acid (2.40 gm, 0.0228 mole). The product (3.5 gm, 45 per cent of theoretical) was best purified by forming the mono-sodium salt with sodium carbonate. The salt separated out at pH 3 (congo red) and was washed to whiteness with chloroform. Acidification yielded 3.0 gm of pure white solid; m.p. 149°. The results were coincident with that of Sharp and Hoffman (18).

Condensation of 1,3-Diphenylpropanetrione-1,2,3 with p-Nitrophenylacetonitrile. Condensation of 1,3-diphenyl triketone with p-nitrophenylacetonitrile was an adaptation of the procedure of Sachs and Herold (14) by Sharp and Hoffman (18). This gave reliable yields of an addition compound.



Reaction in a mixture containing 3.34 gm (0.014 mole) of diphenyl triketone, 2.26 gm (0.014 mole) of p-nitrophenyl-acetonitrile, and 10.0 ml of dry ethanol was initiated by adding 10.0 drops of dry piperidine. The resulting dark red solution, after standing 12.0 hours, produced dark green crystals which were washed satisfactorily with alcohol. The amount of crude product obtained was 3.7 gm, melted from 125-130°, and represented a yield of 66 per cent. Recrystallization was made from ethanol solution brought to turbidity with water. The melting point of this purified substance was 153-155° corresponding to that reported by Sharp and Hoffman (18). However, subsequent recrystallization lowered the melting point to 141-144°.

Condensation Studies Involving 1,3-Diphenylpropanetrione with Various Active Methylene Compounds. A summary of the results obtained in studies dealing with the condensation of 1,3-diphenylpropanetrione-1,2,3 with active methylene compounds is given in Table 2. All condensation experiments utilized only 2.0 gm of the tricarbonyl compound. Consequently, separation and purification techniques were on a semi-micro scale. In general the recovery of starting materials or products was effected by extractions of the reaction mixture dissolved in ethyl acetate or benzene with solutions of sodium bicarbonate or hydrochloric acid. Sublimation techniques were employed to determine benzoic acid in tars and oils. In some cases melting points, and mixed melting points, were used to

identify derivatives of expected fractions. The hydrate of the triketone was recovered by vacuum micro-distillation and subsequently identified by mixed melting point determinations. The hydrate was found to melt over a 25 degree range depending upon the extent of dehydration. All condensations were based on the work of Knoevenagel (6) with slight modifications.

The general method used to effect combination of reactants was as follows. A 15 ml flask was adapted with a three-way stopcock and a side arm leading to a moisture trap and a carbon dioxide trap. A weighed amount of 1,3-diphenylpropanetrione-1,2,3 and a calculated amount of pure, dry methylene compound was introduced into the flask. The system was closed to the air and pure, dry nitrogen was passed through one stopcock opening. Stirring was accomplished magnetically and the temperature controlled by alternate ice and pre-heated baths. After homogeneity had been reached and at a selected temperature, piperidine was injected by means of a hypodermic syringe through the other stopcock opening. Solvents, when used, were also introduced by this injection method. Care was exercised to protect the reaction mixtures from moisture. The progress of the reactions was followed in a limited manner by qualitative detection of carbon dioxide. Thus, reaction conditions were constantly maintained that decomposition was at a minimum. In general, the reactions were stopped by adding a calculated amount of hydrochloric acid and ice. Separation and purification were often a matter of

Table 2. A summary of attempted condensation reactions<sup>1</sup> involving 1,3-diphenylpropanetrione-1,2,3.<sup>2</sup>

No.:	Agent	Solvent:	T : °C.:	Time : (hrs):	Catalyst:	Results
1	Malonic acid	C <sub>5</sub> H <sub>5</sub> N	30	0.5	C <sub>5</sub> H <sub>11</sub> N	Product melting 140°
2	Malonic acid	C <sub>5</sub> H <sub>5</sub> N	100	1.0	C <sub>5</sub> H <sub>11</sub> N	Tars
3	p-Nitro-benzyl-cyanide	C <sub>2</sub> H <sub>5</sub> OH	30	12.0	C <sub>5</sub> H <sub>11</sub> N	Product melting 154-155°
4	p-Nitro-benzyl-cyanide	C <sub>5</sub> H <sub>5</sub> N	100	1.0	C <sub>5</sub> H <sub>11</sub> N	Benzoic acid, tars
5	Acetyl-acetone		60	5.0	C <sub>5</sub> H <sub>11</sub> N	Benzoic acid, oil
6	Acetyl-acetone		30	2.0	C <sub>5</sub> H <sub>11</sub> N	Benzoic acid, trace of an acid melting 150°
7	Ethyl benzoyl-acetate		30	4.0	C <sub>5</sub> H <sub>11</sub> N	Benzoic acid, benzil
8	Ethyl benzoyl-acetate		30	1.0	C <sub>5</sub> H <sub>11</sub> N	Hydrate recovered
9	Cyano-acetic acid		30	0.5	C <sub>5</sub> H <sub>11</sub> N	Inconclusive
10	Cyano-acetic acid	C <sub>5</sub> H <sub>5</sub> N	60	1.0	C <sub>5</sub> H <sub>11</sub> N	Tars, general decomposition
11	Ethyl cyano-acetate		60	0.25	C <sub>5</sub> H <sub>11</sub> N	Starting materials
12	Ethyl cyano-acetate		20	1.0	C <sub>5</sub> H <sub>11</sub> N	Oils

Table 2. (cont.).

No.:	Agent	:Solvent:	T : °C.:	Time : (hrs):	Catalyst:	Results
13	Ethyl aceto- acetate		25	1.0	C <sub>5</sub> H <sub>11</sub> N	Product melting 100-102°
14	Ethyl aceto- acetate	C <sub>5</sub> H <sub>5</sub> N	70	0.5	C <sub>5</sub> H <sub>11</sub> N	Inconclusive
15	Diben- zoyl methane	C <sub>5</sub> H <sub>5</sub> N	20	0.5	C <sub>5</sub> H <sub>11</sub> N	Hydrate recovered
16	Diben- zoyl methane	C <sub>2</sub> H <sub>5</sub> OH	30	12.0	C <sub>5</sub> H <sub>11</sub> N	Benzoic acid, oils
17	∞-Pico- line		50	1.0		Benzil
18	∞-Pico- line		30	1.0	C <sub>5</sub> H <sub>11</sub> N	Product melting 84-85°
19	Fluorene		30	24.0	C <sub>5</sub> H <sub>11</sub> N	Fluorene
20	Fluorene	C <sub>5</sub> H <sub>11</sub> N	30	1.0	C <sub>5</sub> H <sub>11</sub> N	Fluorene
21	Indene		20	0.5	C <sub>5</sub> H <sub>11</sub> N	Product melting 80-81°
22	Indene		100	1.0	C <sub>5</sub> H <sub>11</sub> N	Benzoic acid
23	Nitro- methane		20	0.5	C <sub>5</sub> H <sub>11</sub> N	Oil
24	Nitro- methane		100	1.0	C <sub>5</sub> H <sub>11</sub> N	Tars
25	Benzyl cyanide		100	1.0	C <sub>5</sub> H <sub>11</sub> N	Benzoic acid
26	Benzyl cyanide		20	1.0	C <sub>5</sub> H <sub>11</sub> N	Product melting 80-81°

Table 2. (concl.).

No.:	Agent	Solvent:	T : °C.:	Time : (hrs):	Catalyst:	Results
27	2,4-Dinitro-toluene	C <sub>5</sub> H <sub>5</sub> N	20	0.5	C <sub>5</sub> H <sub>11</sub> N	Hydrate recovered
28	2,4-Dinitro-toluene	C <sub>5</sub> H <sub>5</sub> N	50	1.0	C <sub>5</sub> H <sub>11</sub> N	Benzoic acid, tars

<sup>1</sup> All condensations were modified Knoevenagel type.

<sup>2</sup> 1,3-Diphenylpropanetrione-1,2,3 in mole ratios with the agents listed.

trial and error in finding a selective solvent. A study of yields resulting from some of the condensations has been compiled in Table 3.

Condensation Reaction of 1,3-Diphenylpropanetrione-1,2,3 with Ethyl Acetoacetate. During the course of the investigation many attempts were made to condense, under different conditions, diphenyl triketone with various active methylene type compounds. The following procedure was chosen as representative of these attempts.

A reaction in a mixture containing 1.08 gm (0.008 mole) of ethyl acetoacetate and 2.0 gm (0.008 mole) of diphenyl triketone was initiated by addition of 0.5 ml (0.005 mole) of piperidine. The technique and apparatus have been described before as a general method. All reagents were freshly distilled and dried. The apparatus was dried in an oven at 110°

Table 3. Study of yields involving 1,3-diphenylpropanetrione-1,2,3 with various active methylene agents.

Agent	:gm, mole: of tri- ketone	gm, mole: of agent	ml, mole of piperidine	:Extrac- tion sol- vent	:m.p. of crude product	:gm and percent yield <sup>1</sup>
Ethyl Aceto- acetate	2.00, 0.008	1.08, 0.008	0.50, 0.005	Ethyl acetate	95- 100°	1.00, 32.0
Indene	2.00, 0.008	0.975, 0.008	0.50, 0.005	None	85- 87°	1.20, 40.0
Benzyl Cyanide	3.00, 0.0126	1.48, 0.0126	0.25, 0.0025	Benzene	80- 82°	1.40, 32.0
Malonic Acid	5.43, 0.0228	2.40, 0.0228	3.40, 0.034	Ethyl acetate	140- 149°	3.50, 45.0
p-Nitro benzyl Cyanide	3.34, 0.014	2.26, 0.014	0.25, 0.0025	None	125- 130°	3.70, 66.0
α-Pico line	2.00, 0.008	0.78, 0.008	0.50, 0.005	Ethyl acetate	84- 85°	0.80, 27.8
Acetyl acetone	2.00, 0.008	0.876, 0.008	0.25, 0.0025	Ethyl acetate	140- 150°	0.10, 3.5

<sup>1</sup> Based upon calculated molecular weights corresponding to equimolar addition products.

before use. The temperature of the mixture was kept at 0° until homogeneity was obtained by a magnetic stirrer. At this point the contents of the flask had assumed a light orange color. Stirring was continued while the reaction mixture was allowed to warm up slowly to room temperature. After an hour, with continued stirring, the contents of the flask had assumed a deep orange color and small bubbles were dispersed throughout



the viscous but clear solution. At this time the reaction mixture was poured into a calculated excess of a 10 per cent solution of hydrochloric acid and ice. This solution was stirred for about 15 minutes and a solvent (ethyl acetate) was added in sufficient quantity to extract any solvent-soluble material. This organic layer was separated in a separatory funnel and dried over anhydrous sodium sulfate for 24 hours at 10°. After removal of the sodium sulfate, the solvent was evaporated at room temperature by means of a dry-air aspirator. The resulting heavy oil was crystallized with difficulty by inducing a nucleus in the oil kept at 5° for 72 hours. The crystal growth was then found to be most rapid at 15°. Earlier repeated attempts made under different temperature conditions were ineffective in crystal growth. The pale yellow crystals were filtered, dried on a clay plate and weighed. This crude product (1.0 gm, 32 per cent) melted at 95-100°. Test portions could not be recrystallized since an oil was formed with all common organic solvents. Therefore, the crystals were washed to whiteness by placing them on a Hirsch funnel with suction applied and adding cold ethyl acetate dropwise. This brief contact with the wash solvent removed a yellow oil which could not be crystallized. The resulting white crystals then could be recrystallized from ethyl acetate. The purified product was insoluble in 5 per cent sodium bicarbonate and melted at 100-102°.

Condensation Reaction of 1,3-Diphenylpropanetrione-1,2,3



with Indene. A representative of alternate procedures that was used in condensation attempts was as follows. Freshly distilled diphenyl triketone (2.0 gm, 0.008 mole) was weighed into a clean, dry 25 ml flask. The flask and contents were tightly stoppered and placed in an ice bath. In a similar manner, freshly distilled indene (0.975 gm, 0.008 mole) was introduced into a clean, dry 25 ml flask and stirred with cooling in dry piperidine (0.5 ml, 0.005 mole). The cooled piperidine-indene solution was then poured with rapid stirring into the flask containing the triketone. The resulting mixture was maintained at 0-5° until homogeneity was reached by stirring with a glass rod. The reaction mixture then was allowed to warm slowly to 20° with continuous stirring. After 30 minutes at 20° the contents of the reaction flask were dark red and viscous. At this point 15 minutes stirring in cold 10 per cent hydrochloric acid changed the red mass to a yellow crystalline solid. This solid was filtered, dried on a clay plate and weighed (1.2 gm, 40 per cent). The product was washed well with five portions of 10 per cent sodium bicarbonate (5 ml each) and two portions of water (10 ml each). The yellow crystals were taken up in diethyl ether and subsequently washed using a separatory funnel. No isolable materials were recovered from the wash solutions in this case. The pale yellow crystals were then taken up in acetone at room temperature and the solution brought to turbidity with water. Two differently colored layers of crystals were formed in 12

hours at 5°. The white crystals were separated mechanically from the yellow mass. A repetition of this process of crystallization with acetone and water finally produced pure white crystals melting at 80-81°. A mixed melting point with authentic diphenyl triketone hydrate was 80-81°.

Purification was also accomplished by treating the original crude product with a large excess of water and refluxing on a steam cone until the solution was clear and a yellow oil had formed on the surface. When cooled somewhat the yellow component solidified and was separated by filtration. The yellow gum appeared to be an impure mixture since it could not be crystallized or otherwise purified. Cooling the clear water solution gave pure white crystals with a melting point of 80-81°. The yield, when purified, was 0.95 gm (32 per cent).

Structure Studies on the Condensation Product of 1,3-Diphenylpropanetrione-1,2,3 and p-Nitro Benzyl Cyanide

Several standard analytical procedures were utilized in an attempt to elucidate the structures of condensation products. The results of some of these trials are summarized in Table 4.

Saponification Equivalents. The purified product (0.3323 gm) was dissolved in 27.00 ml of 0.3096 N alcoholic sodium hydroxide solution and heated (2.0 hours) at reflux temperature. Since the resulting solution was dark red it was diluted to 350 ml and the end point of the back titration determined by means of a Beckman pH meter. Back titration required 61.02 ml of

0.1090 N sulfuric acid solution.

$$\begin{aligned}\text{Sap. eq.} &= 0.3323 \times 1000 / (27.00 \times 0.3096 - 61.02 \times 0.1090) \\ &= 195\end{aligned}$$

A second sample (0.1108 gm) of the same product was dissolved in 26.00 ml of 0.3096 N alcoholic sodium hydroxide solution, heated for 2.0 hours and subsequently diluted to 350 ml. Back titration, using a Beckman pH meter, required 68.70 ml of 0.1090 N sulfuric acid solution.

$$\begin{aligned}\text{Sap. eq.} &= 0.1108 \times 1000 / (26.00 \times 0.3096 - 68.70 \times 0.1090) \\ &= 198\end{aligned}$$

Carbonyl Percent. A solution of hydroxylamine hydrochloride containing pyridine, was refluxed (3.5 hours) with 0.2395 gm of the product according to the method described by Siggia (19). The liberated pyridine hydrochloride required 5.95 ml of 0.6289 N alcoholic sodium hydroxide solution. A blank required 2.75 ml of the same base solution. The end point was determined with bromophenol blue indicator. End point readings were taken when the solution just retained a red coloration. This end point was difficult to reproduce due to dichromatic effects. The calculated molecular weight of the product was 400.

$$\begin{aligned}\text{Carbonyl percent} &= 3.20 \times 0.6289 \times 400 \times 100 / 0.2395 \times 1000 \\ &= 193\end{aligned}$$

A second sample (.0803 gm) heated for 1.5 hours, in an experiment designed to eliminate dichromatic effects, utilized the Beckman pH meter. The solution, after dilution to 500 ml

required 44.70 ml of 0.3096 N alcoholic sodium hydroxide solution. A blank required 43.30 ml of the same base solution.

$$\begin{aligned}\text{Carbonyl percent} &= 1.40 \times 0.3096 \times 400 \times 100 / 0.803 \times 1000 \\ &= 216\end{aligned}$$

Structure Studies on the Condensation Product  
of 1,3-Diphenylpropanetrione-1,2,3 and Malonic Acid

A summary of the analytical data determined during the course of the investigation is shown in Table 4.

Carbonyl Percent. According to the method of Siggia (19), 0.1479 gm of the purified acid required 5.50 ml of 0.6402 N sodium hydroxide solution. A blank required 1.50 ml of the same base solution. The two acid functions in the molecule were calculated to require 1.35 ml of the same base solution. The molecular weight of the acid was calculated to be 342.

$$\begin{aligned}\text{Carbonyl percent} &= 2.65 \times 0.6402 \times 342 \times 100 / 0.1479 \times 1000 \\ &= 392\end{aligned}$$

A second sample (0.1252 gm) of the same product required 6.26 ml of 0.6289 N sodium hydroxide solution. The amount of the same base solution used to determine a blank and calculated for the two acid groups was 2.06 ml and 1.20 ml, respectively.

$$\begin{aligned}\text{Carbonyl percent} &= 3.0 \times 0.6289 \times 342 \times 100 / 0.1252 \times 1000 \\ &= 515\end{aligned}$$

Neutral Equivalents. The titrations were made at 0-5°. End points did not fade in 30 minutes. The purified acid

(0.2000 gm) recrystallized from chloroform, required 12.1 ml of 0.0986 N sodium hydroxide solution. A blank required 0.1 ml of the same base solution.

$$\text{Neutral equivalent} = 0.2000 \times 1000 / 12.0 \times 0.0986 = 169$$

A second sample (0.2065 gm) required 12.2 ml and a blank 0.01 ml of 0.0986 N sodium hydroxide solution.

$$\text{Neutral equivalent} = 0.2065 \times 1000 / 12.19 \times 0.0986 = 172$$

The calculated neutral equivalent for  $C_{13}H_{14}O_7$  (on the basis of two acid groups) was 171.

Saponification Equivalents. The purified acid product (0.2000 gm) was dissolved in 25.00 ml of 0.1198 N sodium hydroxide solution and heated for 1 hour under a reflux condenser. Back titration required 10.80 ml of 0.1090 N sulfuric acid solution.

$$\begin{aligned} \text{Sap. eq.} &= 0.2000 \times 1000 / (25.00 \times 0.1198 - 10.80 \times 0.1090) \\ &= 110 \end{aligned}$$

Another sample of the same material (0.2065 gm) was dissolved in 25.00 ml of 0.1198 N sodium hydroxide solution and heated (3 hours) at reflux temperature. Back titration required 8.20 ml of 0.1090 N sulfuric acid solution.

$$\begin{aligned} \text{Sap. eq.} &= 0.2065 \times 1000 / (25.00 \times 0.1198 - 8.20 \times 0.1090) \\ &= 98 \end{aligned}$$

Active Hydrogen. Several attempts to obtain active hydrogen data utilizing the method described by Siggia (19) failed to yield positive results. When the same method was used to determine the percent of carbonyl, negative results were obtained.

Table 4. Summary of analytical data involving malonic acid and p-nitro benzylcyanide with 1,3-diphenylpropanetrione-1,2,3.

Determination	Method	Compound	Results and conditions
Saponification equivalent	Beckman pH titration	$C_{23}H_{16}O_5N_2$	a 195, heated 2.0 hrs b 198, heated 2.0 hrs
Carbonyl percent	Beckman pH titration	$C_{23}H_{16}O_5N_2$	216, heated 1.5 hrs
Carbonyl percent	$HONH_2 \cdot HCl$	$C_{23}H_{16}O_5N_2$	193, heated 3.5 hrs
Carbonyl percent	$HONH_2 \cdot HCl$	$C_{18}H_{14}O_7$	a Negative, heated 1.0 hr b 392, heated 3.0 hrs c 515, heated 5.0 hrs
Carbonyl percent	$CH_3MgI$	$C_{18}H_{14}O_7$	a Negative b Negative c Negative
Neutral equivalent	$NaOH-HCl$ titration	$C_{18}H_{14}O_7$	a 169 b 172
Saponification equivalent	$NaOH-HCl$ titration	$C_{18}H_{14}O_7$	a 98 b 110
Active hydrogen	$CH_3MgI$	$C_{18}H_{14}O_7$	a Negative b Negative c Negative



# Structure Studies of Products Resulting from Various Condensation Reactions

A study of carbon-hydrogen analysis obtained during the course of the investigation has been compiled in Table 5.

Table 5. Summary of carbon-hydrogen analysis of compounds resulting from attempted condensations of 1,3-diphenylpropanetrione-1,2,3 with various active methylene agents.

Agent re- acted with : triketone :	Predicted : compound <sup>1</sup>	:Percent of carbon and hydrogen			
		: Calculated :		Found	
		: C	H :	C	H
Malonic acid	C <sub>18</sub> H <sub>14</sub> O <sub>7</sub>	63.16	4.10	63.38 63.51	4.30 4.45
	C <sub>18</sub> H <sub>12</sub> O <sub>6</sub>	66.67	3.70		
Acetyl acetone	C <sub>20</sub> H <sub>18</sub> O <sub>5</sub>	71.00	5.33	63.97	5.25
	C <sub>20</sub> H <sub>16</sub> O <sub>4</sub>	75.00	5.00		
Ethyl aceto- acetate	C <sub>21</sub> H <sub>20</sub> O <sub>6</sub>	68.48	5.43	68.25 68.49	5.25 5.26
	C <sub>21</sub> H <sub>18</sub> O <sub>5</sub>	72.00	5.14		
$\alpha$ -Pico- line	C <sub>21</sub> H <sub>17</sub> O <sub>3</sub> N	76.13	5.14	67.05	4.42
	C <sub>21</sub> H <sub>15</sub> O <sub>2</sub> N	80.51	4.79		
Indene	C <sub>24</sub> H <sub>18</sub> O <sub>3</sub>	81.36	5.08	70.29 70.13	4.52 4.36
	C <sub>24</sub> H <sub>16</sub> O <sub>2</sub>	85.71	4.76		
Benzyl cyanide	C <sub>23</sub> H <sub>17</sub> O <sub>3</sub> N	77.75	4.79	69.09 69.04	4.74 4.87
	C <sub>23</sub> H <sub>15</sub> O <sub>2</sub> N	81.90	4.45		

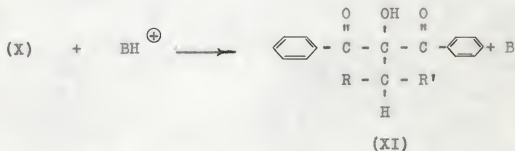
<sup>1</sup> Based upon equimolar addition products and the corresponding unsaturate.



## DISCUSSION AND CONCLUSIONS

The synthesis of 1,3-diphenylpropanetrione-1,2,3 required considerable laboratory time. Although good yields were obtained from all steps involved, the final product proved to be unstable. Decomposition occurred with both the hydrate and the anhydrous triketone. Modifications were made therefore to avoid such decompositions. Attempts were made to eliminate impurities since an irritating vapor was evolved when the tricarbonyl compound decomposed. Therefore, the most logical step in the procedure for investigation was the bromination of dibenzoylmethane and subsequent hydrolysis of the dibromo compound. Near the close of the research, it was found that substitution of an excess of potassium acetate for sodium acetate during the hydrolysis gave a product which did not require recrystallization and was less susceptible to decomposition. Samples of the hydrate resulting from this slight modification were kept three months in open beakers at room temperature without apparent breakdown. Samples resulting from the normal procedure were purified only with difficulty by recrystallization and invariably decomposed. Schonberg (17) observed that the decomposition of diphenyl triketone to benzil was hastened by sunlight. In order to insure a sufficient supply of anhydrous triketone, it was necessary to prepare only small amounts at a time and store them in nitrogen-filled, sealed flasks in the dark at 0°.

The condensation of 1,3-diphenylpropanetrione-1,2,3 with active methylene compounds and catalyzed by a base may be explained in the following manner:



The limiting form (IX) of diphenyl triketone has three positions of positive charge which would be susceptible to an attack by a nucleophilic particle. The selectivity of the medial carbonyl group to such an attack has been proposed by

Sharp and Hoffman (18). The unsaturated benzene rings could furnish electrons to the end carbons, thus diminishing their tendency for normal carbonyl activity. The positive charges on the benzene nucleus could be distributed throughout this highly resonant group and thereby leave only the central carbonyl group open for the postulated nucleophilic attack. The active methylene compound is changed to an anionic particle (VIII) with the removal of a proton by the base. Subsequently the condensation is effected by union of the oppositely charged centers and the proton adds to the anion (IX) which regenerates the catalyst and gives the product (XI).

In addition to electronic effects, the investigation was concerned with relative reactivities of various active methylene compounds, steric hindrance and rearrangements. The postulated point of reaction of the diphenyl triketone is flanked by benzoyl groups which are considered quite bulky. The different substituents of the methylene agents used could also exhibit steric hindrance to condensations. Many methylene agents were eliminated from usage because a weak base would not, in all probability, pull the required proton off. Although many of the methylene agents have been reported to condense with aldehydes, no correlation could be drawn from the experimental evidence that would indicate enhanced reactivity of the medial carbonyl group of the diphenyl triketone.

Kohler and Erickson (9) reported that phenylmagnesium halide reacted with diphenyl triketone to give a rearranged

product instead of the normal addition compound. A possible mechanism of this rearrangement as applied to condensation reactions could involve the following electronic shifts:



Malonic acid was condensed with 1,3-diphenylpropanetrione-1,2,3 and the product gave neutral equivalent and carbon-hydrogen data coincident with those of Sharp and Hoffman (18) for  $\text{C}_{18}\text{H}_{14}\text{O}_7$ . Attempts to obtain carbonyl per cent and active hydrogen data were unsatisfactory. It is conceivable that the neighboring influence of functional groups and steric hindrance could cause irregular behavior of the entire molecule. Attempts to find suitable conditions for the reactions were finally abandoned.

Para-nitrobenzyl cyanide was condensed with 1,3-diphenylpropanetrione-1,2,3. Additional evidence was found to support

the carbon-hydrogen data reported by Sharp and Hoffman (18) for the proposed addition compound,  $C_{23}H_{16}O_5H_2$ . Saponification equivalents were approximately one-half of the molecular weight. The conditions of the reaction produced two acid groups which would be logically benzoic acid and the acid resulting from hydrolysis of the nitrile. No attempt was made to prove this since the course of the investigation was directed otherwise. Independent methods indicated two carbonyl groups were present in the condensation compound. This agrees with structure XI.

A Beckman Model G pH meter was utilized in obtaining analytical data for the condensation product of p-nitrobenzyl cyanide and diphenyl triketone. The use of such an instrument is necessary since the compound in basic solution, turned a deep red color that masked the color change of an organic indicator. In addition, the use of bromphenol blue indicator was hampered by dichromatic effects. Blank determinations were made with each sample. The curves obtained were those of a strong acid-strong base type expected from a normal titration. The method was found to be desirable since the instrument readings were affected only by the concentration of the hydrogen ions.

It has been pointed out in the introduction that diphenyl triketone is very sensitive to basic conditions and high temperatures necessary for normal condensation. The failure of many condensation reactions summarized in Table 2 is probably

caused by these sensitivities. In the cases where ethyl benzoylacetate, dibenzoyl methane, and 2,4-dinitrotoluene were held at or near room temperature, the hydrate of the diphenyl triketone was recovered unchanged from the reaction mixtures. In the reaction of fluorene with diphenyl triketone at 30°, fluorene was recovered in almost quantitative yield and indicates that no reaction occurred. When reaction temperatures were raised to around 50°, either expected degradation products or oils resulted from trials involving acetyl acetone, cyanoacetic acid, ethyl cyanoacetate, alpha-picoline, and 2,4-dinitrotoluene. In all cases tars were formed when the temperature was maintained above 60°. Since the temperature of the condensations were limited and only a weakly basic catalyst allowed, the success of the reactions could depend upon the activity and size of the active methylene component.

Products other than those expected from degradations of starting materials were isolated from reactions involving ethyl acetoacetate, indene, benzyl cyanide, alpha-picoline and acetyl acetone. All of these products resulted from reactions at room temperature or less. It was found that reactants mixed at ice-bath temperature and allowed to warm up slowly to around 30° gave best results. Further, the optimum time of reactions was determined experimentally to be not over one hour. The solvent most suitable for extraction was ethyl acetate. The suitability of this solvent was due probably to the fact that it apparently did not carry over trace amounts of the



salts of pyridine and piperidine.

The course of the reactions was not completely illuminated and no mechanisms other than those previously suggested are offered. The carbon-hydrogen data resulting from various condensations have been compiled in Table 4. This evidence alone does not warrant extensive supposition concerning fine molecular structure.

Reversibility of similar condensation reactions was observed by Kohler and Corson (8). Addition of ice and hydrochloric acid at the completion of the reaction was expected to prevent this. The acid removed the basic catalyst and the basic solvent by forming the corresponding non-basic salt. In accordance with the results of Sharp and Hoffman (18) a long reaction time decreased yields of a similar condensation.

The condensation products were difficult to separate and purify. Several of them formed a heavy oil with all organic solvents employed and considerable manipulation at various temperatures was necessary to induce crystallization. It was reasoned that this tendency to form an oil was associated with impurities since second and third recrystallizations were normal. However, a few compounds even when pure were found difficult to crystallize. In general no common solvent or other method of purification was discovered. Trial and error in selection of a solvent was necessary. Manipulations were tedious due to small amounts of products caused by the limited avail-



ability of diphenyl triketone.

The condensation reactions between the diphenyl triketone and active methylene compounds were modifications of the procedures of Knoevenagel (6). The products expected would be equimolar additions or the corresponding tetra-substituted ethylene resulting from the loss of a molecule of water.

#### SUMMARY

Diphenyl triketone reacted with malonic acid, para-nitro benzyl cyanide, ethyl acetoacetate, indene, benzyl cyanide, acetylacetone and alpha-picoline to give insoluble products. Many other compounds containing active methylene groups did not appear to react under the piperidine-catalyzed reaction conditions.

Evidence was found which supported the formula  $C_{18}H_{14}O_7$  for the condensation product of 1,3-diphenylpropanetrione-1,2,3 and malonic acid.

The formula  $C_{23}H_{16}O_5N_2$ , postulated for the condensation of 1,3-diphenylpropanetrione-1,2,3 and para-nitro benzyl cyanide, was also supported by experimental evidence.

Other products were investigated only by carbon-hydrogen analysis. No further interpretation was given.

It is possible that steric hindrance and too sensitive reaction conditions caused the failure of diphenyl triketone to condense with many other active methylene compounds. It is

also possible that a stronger base than piperidine could be used, in order to pull the required proton from the reagent containing the methylene group. However, such stronger bases in all likelihood would destroy the diphenyl triketone. The experimental evidence does not contradict the supposition that the central carbonyl group of diphenyl triketone is selectively reactive towards attack by a nucleophilic particle.

## ACKNOWLEDGMENTS

The author wishes to express his indebtedness to society for the moral, spiritual and financial assistance which has culminated in the production of this thesis. The excellence of the technical aid offered by the Department of Chemistry is duly recognized and appreciated. Dr. Dexter B. Sharp, by his determined scientific endeavor, contributed guidance which proved exemplary and worthwhile to the author.

## LITERATURE CITED

- (1) Allen, C. F. H.  
Dibenzoylmethane. Organic synthesis. 8: 60-62.  
New York: John Wiley and Sons. 1928.
- (2) Bigelow, L. A., and R. S. Hanslick.  
Diphenyl triketone. Organic synthesis. 13: 38-40.  
New York: John Wiley and Sons. 1933.
- (3) Bigelow, L. A., H. G. Rule, and W. A. P. Black.  
The catalytic hydrogenation of diphenyl triketone.  
Jour. Chem. Soc. (London). p. 83-85. 1935.
- (4) Bouveault, L.  
Preparation of 1,2-diketobutyric ester. Bull. Soc.  
Chem. (3)33:475-481. 1903. Jour. Chem. Soc.  
(London) Abstr. 11, 1904. p. 588.
- (5) Bouveault, L. and A. Wahl.  
Sur les ethers isonitrosomaloniques et leur trans-  
formation en ethers mesoxaliques. Compt. rend.  
137: 196-198. 1903.
- (6) Knoevenagel, E.  
Condensation von Malonsaure mit aromatischen  
Aldehyden durch Ammoniak und Amine. Ber. der  
Deutsch. Chem. Gesell. 31: 2596-2619. 1898.
- (7) Kohler, E. P. and H. M. Chadwell.  
Benzalacetophenone. Organic synthesis. 2: 1-3.  
New York: John Wiley and Sons. 1922.
- (8) Kohler, E. P. and B. B. Corson.  
The mechanism underlying the reaction between  
aldehydes or ketones and tautomeric substances of  
the keto-enol type. Amer. Chem. Soc. Jour. 45:  
1975-1986. 1923.
- (9) Kohler, E. P. and J. L. E. Erickson.  
The cleavage of beta-diketones I. Cleavage by  
organic magnesium compounds. Amer. Chem. Soc. Jour.  
53: 2301-2309. 1931.
- (10) de Neufville, R. and H. von Peckmann.  
Über das Diphenyltriketone. Ber. der Deutsch. Chem.  
Gesell. 23: 3375-3379. 1890.

- (11) Sachs, F. and H. Barschall.  
Über Triketone. I. Ber. der Deutsch. Chem. Gesell.  
34: 3047-3052. 1901.
- (12) Sachs, F. and A. Rohmer.  
Über Triketone. II. Ber. der Deutsch. Chem.  
Gesell. 35: 3307-3312. 1902.
- (13) Sachs, F. and W. Wolff.  
Über Triketone. III. Ber. der Deutsch. Chem.  
Gesell. 36: 3221-3236. 1903.
- (14) Sachs, F. and V. Harold.  
Über Triketone. IV. Ber. der Deutsch. Chem.  
Gesell. 40: 2714-2730. 1907.
- (15) Schmitt, G.  
Concerning the products of condensation of mesoxalic  
esters and oxalacetic esters with cyano-acetic esters.  
Ann. chim. et. phys. 12: 406-432. 1908.
- (16) Schonberg, A. and R. C. Azzam.  
Abnormal action of acids on 1,2,3-triketones. Jour.  
Chem. Soc. (London). p. 1428-2430. 1939.
- (17) Schonberg, A.  
Degradation reactions in organic chemistry. Nature.  
142: 997. 1938.
- (18) Sharp, D. B. and H. A. Hoffman.  
The chemistry of vicinal tricarbonyl compounds. I.  
Condensation reaction of 1,3-diphenylpropanetrione-  
1,2,3. Amer. Chem. Soc. Jour. 72: 4311. 1950.
- (19) Siggia, S.  
Quantitative organic analysis via functional groups.  
New York: John Wiley and Sons. 1949.
- (20) Wahl, M. A.  
Sur le benzoylglyoxalate d'ethyle. Compt. rend.  
144: 211-214. 1907.

CONDENSATION OF 1,3-DIPHENYLPROPANETRIONE-1,2,3  
WITH ACTIVE METHYLENE COMPOUNDS

by

ROBERT ELLIOTT YEAGER

B. A., Southwestern College, Winfield, 1950

---

AN ABSTRACT OF A THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Chemistry

KANSAS STATE COLLEGE  
OF AGRICULTURE AND APPLIED SCIENCE

1952

Experiments were designed to afford a study of condensation reactions of the Knoevenagel type involving 1,3-diphenylpropane-trione-1,2,3 with active methylene compounds. Attention was also directed towards structure proofs of products obtained.

According to modern electronic interpretations of organic chemistry, the central carbonyl group of diphenyl triketone would be selectively reactive to an attacking nucleophilic reagent. The general purpose of the investigation was to obtain experimental evidence which would aid in advancing chemistry concerned with electronic theories.

A slight modification was made in the standard method for preparing diphenyl triketone which resulted in a purer, more stable product. An exhaustive examination of the reaction involved was not attempted.

Diphenyl triketone was found to react with malonic acid, para-nitro benzyl cyanide, ethyl acetoacetate, indene, benzyl cyanide, acetylacetone and alpha-picoline. Many other compounds containing active methylene groups did not appear to react under the piperidine-catalyzed reaction conditions.

The formula,  $C_{18}H_{14}O_7$  for the condensation product of diphenyl triketone and malonic acid was supported by carbon-hydrogen analysis and neutral equivalents. Attempts to obtain other analytical data were not successful.

Carbonyl percents and saponification equivalents were found to support the formula  $C_{23}H_{16}O_5N_2$ , postulated for the condensation of diphenyl triketone and para-nitro benzyl



cyanide.

Other products were investigated only by carbon-hydrogen analysis. No further interpretation was given.

It is possible that steric hindrance and too sensitive reaction conditions caused the failure of diphenyl triketone to condense with many other active methylene compounds. It is also possible that a stronger base than piperidine could be used, in order to pull the required proton from the reagent containing the methylene group. However, such stronger bases in all likelihood would destroy the diphenyl triketone. The experimental evidence does not contradict the supposition that the central carbonyl group of diphenyl triketone is selectively reactive towards attack by a nucleophilic particle.